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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,420	11/26/2003	Stanley Beames Brown	0001530USQ/3049	2642

23117 7590 06/25/2007

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
06/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,420	BROWN ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *77-79,84,89-91 and 98-100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77-79,84,89-91,98-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 77-79, 84, 89-91 and 98-100 are presented for examination.

Applicant is notified that the finality of the previous Office Action dated March 28, 2007 is hereby withdrawn. The after-final amendment filed May 17, 2007 has been entered into the record and prosecution of the present application has been reopened.

Applicant's after-final amendment filed May 17, 2007 has been received and entered into the instant application. Claims 77-79, 84, 89-91 and 98-100 are pending and under examination. Claims 77, 79, 84, 89 and 100 are amended. Claims 44-53, 65-76, 80-83, 85-88, 92, 94 and 96-97 are cancelled.

Applicant's amendments and remarks, filed May 17, 2007, have been fully considered. Regrettably, however, the allowability of the instant claims is hereby **withdrawn** upon reconsideration of the present claim set. Accordingly, the following rejections are newly applied and constitute the complete set of rejections applied to the instant claims.

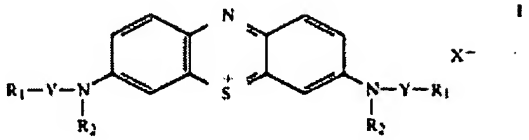
Claim Rejections - 35 USC § 102 (New Grounds of Rejection)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 79 is rejected under 35 U.S.C. 102(b) as being anticipated by Mazur et al. (U.S. Patent No. 5,220,009; 1993).

Mazur et al. teaches the use of 3,7-disubstituted phenothiazinium salts for the photochemical disinfection of aqueous effluents (abstract), wherein the phenothiazinium salts are of the formula:



wherein:
either R_1 is a saccharide residue;
R_2 is alkyl, cycloalkyl, aryl, aralkyl or heterocyclyl, any alkyl or alkylene chain being optionally interrupted by one or more heteroatoms, and Y is alkylene optionally substituted by alkyl, cycloalkyl, aryl or aralkyl; or
R_1 and R_2 are each methyl and Y is a bond; and when R_1 is a saccharide residue X is an anion selected from halogen, $R_3CO_2^-$, $R_3SO_3^-$ and $R_3OSO_3^-$, wherein R_3 is alkyl, cycloalkyl, aryl, aralkyl or heterocyclyl, and
when R_1 and R_2 are each methyl, X is an anion selected from $R_3SO_3^-$, $R_3OSO_3^-$ wherein R_3 is as defined above and $R_4CO_2^-$, wherein R_4 is an aldose or ketose residue, an N-protected α-amino acid residue or a ω-carboxy-α-amino acid residue.

(abstract and col.1, l.54-col.2, l.12). Mazur et al. exemplifies specific compounds of formula (I), e.g., compound Ia (3,7-Bis-(N-methyl-N-beta-glucopyranosylethylamino)-phenothiazin-5-ium bromide; corresponds to Applicant's claimed compounds wherein X is a bromide counteranion, p is 1, A and B are both –NR'R'', and R' is methyl and R'' is an optionally substituted linear hydrocarbon group), and further teaches the addition of compound (Ia) to unchlorinated effluent from an activated sludge treatment plant that contained non-soluble fecal coliforms (i.e., *E.coli*; col.5, l.15-25) and exposing the solution to visible light radiation (Example 12), which resulted in a significant decrease in colony forming units of the fecal coliform microorganisms, in fact, a more significant decrease than conventional methylene blue (see comparative data presented in Table 4, col.9).

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 79 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner (WO 91/16911; 1991) in light of *The Merck Index* (Monograph 5979, 1989), cited to show a fact, in view of Wainwright et al. ("Photobactericidal Activity of Phenothiazinium Dyes Against Methicillin-Resistant Strains of *Staphylococcus aureus*", *FEMS Microbiology Letters*, 160(1998):177-181) and Shanbrom (U.S. Patent No. 6,183,764; 2001).

Wagner teaches a method for decontaminating blood or cellular blood components (p.6, l.7-9) comprising the addition of methylene blue (a phenothiazin-5-ium dye; p.6, l.9-11, p.8, l.3-5) in an effective concentration acceptable for transfusion, such that the treated blood or blood component does not require additional manipulation to remove the dye (p.15, l.4-15) and then treating said blood or blood components with light at an effective wavelength and intensity, wherein the light is absorbed by said dye and results in the inactivation of pathogenic contaminants (p.6, l.11-25), such as, e.g., bacterial species such as *Streptococcus* species or *Escherichia* species (p.10, l.22-25).

Wainwright et al. is cited for its teaching of the antibacterial properties of methylene blue against *S. aureus* and methicillin-resistant *S. aureus* (see Table 2, p.179). In view of such teachings, one of skill in the art at the time of the invention would have had a reasonable expectation of success in using the methylene blue dye of Wagner for disinfecting the disclosed blood or blood components from *S. aureus*

and methicillin-resistant *S. aureus* based on the bactericidal activity of methylene blue against such bacteria as evidenced by Wainwright et al.

Shanbrom (U.S. Patent No. 6,183,764; 2001) is cited for its teachings of an organic polymer material to which is tightly adsorbed a disinfectant organic dye (abstract, l.1-5), such as methylene blue (col.2, l.30-40). Shanbrom teaches the exposure of squares of polyvinylchloride treated with methylene blue and gentian violet to blood or plasma as the microbial growth medium and reported effective microbicidal activity (col.4, l.8-31). Shanbrom discloses that the unusual effectiveness of the polymer-dye material was most likely due to the adsorption of the dye to the polymer, which prevents it from washing away and becoming too dilute to be effective (col.4, l.46-49).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to employ a dye compound, such as the methylene blue dye disclosed by Wagner, in conjunction with a polymeric material for the sterilization of fluids, such as the blood or blood products disclosed in Wagner. Such a person would have been motivated to employ a dye-polymer combination because the teachings of Shanbrom raise the reasonable expectation of success that the use of the disinfectant dye in combination with a polymer would have exerted an increased and prolonged anti-microbial effect of the compound because the presence of the polymer would increase the resident time of the microbicidal dye compound in the blood or blood component by resisting dilution of the dye to the point of inactivating its antimicrobial effect.

Though Wagner, Wainwright and Shanbrom are directed to the use of methylene blue (see *The Merck Index* (1989), which shows that methylene blue is of the identical core structure as that presented as Formula (I) in present claim 79, wherein R' and R'' are both methyl moieties) and not a phenothiazine dye excluding compounds wherein A and B are both either (-N(CH3)2) or (-N(CH2CH3)2) as presently claimed, the use of a compound homologous to methylene blue that solely differs in the length of the hydrocarbon chain (i.e., wherein the two methyl groups are substituted by, for example, two propyl

groups, or two butyl groups, etc.) and, therefore, would share significant structural homology to methylene blue *per se,* would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention. Such a person would have been motivated to use such a compound(s) with a reasonable expectation of success in achieving the same, or substantially similar therapeutic benefit to the patient, because the shared structural similarities and, thus, homology between the compounds, would have reasonably predicted that the compounds would have shared similar pharmacologic properties due to their homologous chemical structures. It has long been held in patent law that a *prima facie* case of obviousness may be based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound, such as homology or position isomerization. Please see *In re Deuel*, 34 USPQ2d at 1214. The necessary motivation to make a claimed compound and, thus, the *prima facie* case of obviousness, rises from the reasonable expectation that compounds similar in structure will have similar properties. Please see *In re Gyurik*, 596 F.2d.1012, 201 USPQ 552 (CCPA 1979) and *In re Grabiak*, 226 USPQ 870. Please also see MPEP §2144.09, which states that compounds that are homologs (e.g., compounds differing regularly by the successive addition of the same chemical group, e.g., by –CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties.

Furthermore, the reasonable expectation of similar pharmacologic properties of phenothiazinium compounds with extended hydrocarbon chain substitutions would also have suggested to one of ordinary skill in the art at the time of the invention that such compounds would also have exhibited bactericidal activity against *S. aureus* and methicillin-resistant *S. aureus* similar to that of methylene blue *per se*, absent factual evidence to the contrary.

Claims 77, 79, 89-91 and 98-99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al. (U.S. Patent No. 5,611,793; 1997) in light of *The Merck Index* (Monograph 5979,

1989), cited to show a fact, in view of Biel (WO 01/62289; 2001) and Wainwright et al. ("Photobactericidal Activity of Phenothiazinium Dyes Against Methicillin-Resistant Strains of *Staphylococcus aureus*", *FEMS Microbiology Letters*, 160(1998):177-181).

Wilson et al. teaches a method for disinfecting (col.1, l.28-30) or sterilizing tissues or a wound or lesion (col.1, l.28-30) in the oral cavity of a patient comprising the topical application (col.1, l.28-34, col.4, l.55-65) of a photosensitizing compound (col.1, l.28-34, col.2, l.37-62), such as, e.g., methylene blue (col.2, l.46), to the tissues, wound or lesion and irradiating the tissues, wound or lesion with laser light at a wavelength absorbed by the photosensitizing compound (col.1, l.28-34), wherein the method may be used for the destruction of disease-related microbes related to chronic periodontitis and gingivitis (col.2, l.1-7), cariogenic microbes on a tooth surface in order to treat or prevent dental caries (col.2, l.10-11), or treatment of oral candidiasis (col.2, l.14-16).

Biel (WO 01/62289; 2001) is cited for its teachings of the antimicrobial properties of methylene blue when activated via light against *Candida albicans, Eschericia coli, Pseudomonas aeruginosa* and *Staphyloccocus aureus* (Figure 2). In view of such teachings, one of skill in the art at the time of the invention would have had a reasonable expectation of success in using the methylene blue dye of Wilson et al. for the claimed methods of disinfection to treat *Candida albicans, Eschericia coli, Pseudomonas aeruginosa* and *Staphyloccocus aureus* in the disclosed tissues, wounds or lesions based on the microbicidal activity of methylene blue against such microorganisms as evidenced by Biel.

Further, Biel teaches the compatibility of methylene blue in both oral and intravenous administration and additionally teaches that methylene blue has very low tissue toxicity and can be administered to human orally and intravenously in high doses without any toxic effects (see paragraph bridging p.6-7). Thus, while Wilson et al. teaches the topical administration of the disclosed photosensitizing composition, it would have been *prima facie* obvious to one of ordinary skill in the art to adapt the therapy for either oral or intravenous administration (i.e., systemic) of the photosensitizing dye

compound, since the dyes of Wilson et al. were known to be amenable to such formulations and would not have exerted undue toxicity on surrounding tissues or the subject as a whole. In addition, the skilled artisan would have determined the optimal route of administration based upon a variety of factors, including, but not limited to, the dosage amount to be administered, the frequency and ease of administration, the site to be treated, the severity of disease and patient compliance with the regimen. In the absence of evidence to the contrary, the currently claimed routes of administration are not seen to be inconsistent with those that were commonly used in the art to administer such dye compounds and also are not seen to be inconsistent with those that would have naturally commended themselves to one of ordinary skill in the art at the time of the invention. Moreover, the skilled artisan would have reasonably expected to retain the microbicidal activity of the composition, regardless of the formulation, absent factual evidence or direction to the contrary.

Wainwright et al. ("Photobactericidal Activity of Phenothiazinium Dyes Against Methicillin-Resistant Strains of *Staphylococcus aureus*", *FEMS Microbiology Letters*, 160(1998):177-181) is cited for its teaching of the antibacterial properties of methylene blue against *S. aureus* and methicillin-resistant *S. aureus* (see abstract and Table 2, p.179) and further teaches and suggests that staphylococcal infections or colonization found in epidermal wounds or burns may be accessible to topical treatment with such bactericidal agents (col.1, second paragraph, p.178). In view of such teachings, one of skill in the art at the time of the invention would have had a reasonable expectation of success in using the methylene blue dye of Wilson et al. for the claimed methods of disinfection of oral tissues, wounds or lesions or epidermal or burn wounds to treat *S. aureus* and methicillin-resistant *S. aureus* based on the bactericidal activity of methylene blue against such bacteria as evidenced by Wainwright et al.

Though Wilson et al., Biel, and Wainwright et al. are directed to the use of methylene blue (see *The Merck Index* (1989), which shows that methylene blue is of the identical core structure as that presented as Formula (I) in present claim 79, wherein R' and R'' are both methyl moieties) and not a

phenothiazine dye excluding compounds wherein A and B are both either (-N(CH3)2) or (-N(CH2CH3)2) as presently claimed, the use of a compound homologous to methylene blue that solely differs in the length of the hydrocarbon chain (i.e., wherein the two methyl groups are substituted by, for example, two propyl groups, or two butyl groups, etc.) and, therefore, would share significant structural homology to methylene blue *per se,* would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention. Such a person would have been motivated to use such a compound(s) with a reasonable expectation of success in achieving the same, or substantially similar therapeutic benefit to the patient, because the shared structural similarities and, thus, homology between the compounds, would have reasonably predicted that the compounds would have shared similar pharmacologic properties due to their homologous chemical structures. It has long been held in patent law that a *prima facie* case of obviousness may be based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound, such as homology or position isomerization. Please see *In re Deuel*, 34 USPQ2d at 1214. The necessary motivation to make a claimed compound and, thus, the *prima facie* case of obviousness, rises from the reasonable expectation that compounds similar in structure will have similar properties. Please see *In re Gyurik*, 596 F.2d.1012, 201 USPQ 552 (CCPA 1979) and *In re Grabiak*, 226 USPQ 870. Please also see MPEP §2144.09, which states that compounds that are homologs (e.g., compounds differing regularly by the successive addition of the same chemical group, e.g., by –CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties.

Furthermore, the reasonable expectation of similar pharmacologic properties of phenothiazinium compounds with extended hydrocarbon chain substitutions would also have suggested to one of ordinary skill in the art at the time of the invention that such compounds would also have exhibited bactericidal activity against *Candida albicans, Eschericia coli, Pseudomonas aeruginosa* and *Staphyloccocus aureus*

and methicillin-resistant *S. aureus* similar to that of methylene blue *per se*, absent factual evidence to the contrary.

Claims 77, 79, 89-91 and 98-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al. (U.S. Patent No. 5,611,793; 1997) in light of *The Merck Index* (Monograph 5979, 1989), cited to show a fact, in view of Biel (WO 01/62289; 2001) and Wainwright et al. ("Photobactericidal Activity of Phenothiazinium Dyes Against Methicillin-Resistant Strains of *Staphylococcus aureus*", *FEMS Microbiology Letters*, 160(1998):177-181), and further in view of Chowdhary et al. (U.S. Patent Application Publication No. 2002/0061330; 2002).

Wilson et al., *The Merck Index*, Biel and Wainwright et al. as applied above.

Chowdhary et al. (U.S. Patent Application Publication No. 2002/0061330; 2002) is cited for its teaching of photosensitizing compositions, such as, e.g., phenothiazinium compounds (para.[0039], p.4; see also para.[0049], p.7, which discloses methylene blue and derivatives thereof), in combination with a polymeric carrier agent (para.[0089], p.13), which may be applied as topical and mucosal copolymer formulated preparations for the treatment of psoriatic lesions (para.[0112], p.16), and which is activated via exposure to light (para.[0145-0146], p.18-19).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to use the disclosed methylene blue dye compound of Wilson et al., or structurally homologous compounds (i.e., those with extended hydrocarbon chain substitutions as discussed *supra*) for the treatment of psoriatic lesions as disclosed by Chowdhary et al. with a reasonable expectation of success because Chowdhary et al. expressly discloses the amenability of such lesions to treatment via photodynamic therapy using phenothiazinium-based photosensitizing compounds, such as, e.g., methylene blue-type compounds, exposed to light. Furthermore, the reasonable expectation of similar pharmacologic properties of phenothiazinium compounds with extended hydrocarbon chain substitutions

(as compared with the methylene-blue type compounds disclosed by Chowdhary et al.) would also have suggested to one of ordinary skill in the art at the time of the invention that such compounds would also have exhibited similar efficacy in treating psoriatic lesions similar to that of methylene blue, absent factual evidence to the contrary.

Double Patenting (New Grounds of Rejection)

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Provisional Rejection

Claims 77-79, 89-91 and 98-100 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-8 of copending U.S. Patent Application No. 11/723,523 in light of *The Merck Index* (Monograph 5979, 1989), cited to show a fact, in view of Biel (WO 01/62289; 2001), Wainwright et al. ("Photobactericidal Activity of Phenothiazinium Dyes Against Methicillin-Resistant Strains of *Staphylococcus aureus*", *FEMS Microbiology Letters*, 160(1998):177-181) and Chowdhary et al. (U.S. Patent Application Publication No. 2002/0061330; 2002).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference

claims.

Although the conflicting claims are not identical, the claims of the instant patent application and those of the cited copending applications are not considered patentably distinct from each other because the pending claims are rendered obvious by the copending claims.

The copending claims of clearly provide for phenothiazinium compounds of an identical core structure to that presently claimed, wherein moieties A and B can be selected from –NR7R8, further wherein R7 and R8 are each independently selected from hydrogen and optionally substituted C1-C6 alkyl, for the treatment of wound healing by applying or administering the compound and exposing the wound area to light.

The Merck Index is cited to show that the compound methylene blue corresponds to the structure of the copending claims, wherein A and B are –NR7R8 and both R7 and R8 are each methyl groups and Y is a chloride counteranion and p is 1.

One of ordinary skill in the art would have been motivated to use the copending phenothiazinium compounds for the treatment of wounds infected with *Candida albicans, Eschericia coli, Pseudomonas aeruginosa* and *Staphyloccocus aureus* because Biel (WO 01/62289; 2001) teaches the antibacterial properties of methylene blue when activated via light against *Candida albicans, Eschericia coli, Pseudomonas aeruginosa* and *Staphyloccocus aureus* (Figure 2). In view of such teachings, one of skill in the art at the time of the invention would have had a reasonable expectation of success in using the methylene blue dye of the copending claims for treating wounds infected with *Candida albicans, Eschericia coli, Pseudomonas aeruginosa* and *Staphyloccocus aureus* in a subject based on the bactericidal activity of methylene blue against such microorganisms as evidenced by Biel.

Further, one of ordinary skill in the art would have been motivated to use the copending phenothiazinium compounds for the treatment of wounds, especially epidermal or burn wounds, infected with methicillin-resistant *Staphyloccocus aureus* because Wainwright et al. ("Photobactericidal Activity

of Phenothiazinium Dyes Against Methicillin-Resistant Strains of *Staphylococcus aureus*", *FEMS Microbiology Letters*, 160(1998):177-181) teaches the antibacterial properties of methylene blue against *S. aureus* and methicillin-resistant *S. aureus* (see abstract and Table 2, p.179) and further teaches and suggests that staphylococcal infections or colonization found in epidermal wounds or burns may be accessible to topical treatment with such bactericidal agents (col.1, second paragraph, p.178). In view of such teachings, one of skill in the art at the time of the invention would have had a reasonable expectation of success in using the methylene blue dye of the copending claims for treating wounds (including burn wounds) infected with *S. aureus* and methicillin-resistant *S. aureus* in a subject based upon the bactericidal activity of methylene blue against such microorganisms as evidenced by Wainwright et al.

Moreover, one of ordinary skill in the art would have been motivated to use the copending phenothiazinium compounds for the treatment of psoriatic lesions because Chowdhary et al. (U.S. Patent Application Publication No. 2002/0061330; 2002) expressly teaches photosensitizing compositions, such as, e.g., phenothiazinium compounds (para.[0039], p.4; see also para.[0049], p.7, which discloses methylene blue and derivatives thereof), in combination with a polymeric carrier agent (para.[0089], p.13), which may be applied as topical and mucosal copolymer formulated preparations for the treatment of psoriatic lesions (para.[0112], p.16), and where the compound is activated via exposure to light (para.[0145-0146], p.18-19). In view of such teachings, one of skill in the art at the time of the invention would have had a reasonable expectation of success in using the methylene blue dye of the copending claims for the treatment of psoriatic lesions, since Chowdhary et al. discloses the amenability of such lesions to treatment via photodynamic therapy using phenothiazinium-based photosensitizing compounds (such as, e.g., methylene blue).

Though the copending claims are directed to phenothiazinium compounds other than methylene blue, specifically, wherein R7 and R8 may be C2-C6 alkyl groups, the structural homology between methylene blue and phenothiazinium compounds with extended hydrocarbon chains (i.e., a C2-C6 alkyl)

would have raised the reasonable expectation of success that such homologous compounds would have exhibited similar pharmacologic properties, absent factual evidence to the contrary. Furthermore, though the instant claims exclude methylene blue *per se*, the instant claims recite other structural homologs of methylene blue (i.e., those with longer carbon chains, such as, e.g., butyl, instead of methyl) that clearly overlap with those of the copending claims, which, given the reasonable expectation of similar pharmacologic properties, renders the instant claims obvious over the copending claims.

Accordingly, rejection of claims 77-79, 89-91 and 98-100 is proper over claims 7-8 of copending U.S. Patent Application No. 11/723,523 as claiming obvious and unpatentable variants thereof. This is a provisional rejection because the claims have not yet, in fact, been patented.

Conclusion

Rejection of claims 77-79, 84, 89-91 and 98-100 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit 1614

June 16, 2007

6/20/07
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